## REMARKS

Claims 3-7 are pending and Claims 11-31 are withdrawn from consideration and canceled. Claims 1-2 and 8-10 have also been canceled.

The support for the claim amendments are as follows: Claim 3: (claims 9 and 10; p.15, lines 5-11 and p.22, line 18 to p.23, line 2) and claims 4-7: (dependency changed to claim3). The applicants respectfully submit that no new matter has been added. It is believed that this Amendment is fully responsive to the Office Action dated August 3, 2006.

**The application fails to comply with the requirements of 37 CFR §§ 1.821 – 1.825. Applicant is required to either amend the Figures with the corresponding SEQ ID numbers or alternatively applicant may amend the Brief Description of the Figures (beginning at page 12 of the specification) with the corresponding SEQ ID numbers.** (Office Action p.3)

The Brief Description of the Figures has been amended with corresponding SEQ ID numbers as suggested by the Examiner to overcome the objection.

**The disclosure is objected to because of the following informalities: There are several instances within the specification wherein the symbol of a filled square (e.g., ■), designating a particular group in the corresponding drawings is instead denoted as a "|".** (Office Action p.3)

The specification has been corrected as suggested by the Examiner to overcome the objection.

**Claims 1-10 are objected to because of the following informalities: claims 1-6 recite the phrase "the amino acid sequence resulted from a partial alteration...", wherein the word "resulted" is grammatically awkward.** (Office Action p.4)

The objectionable language has been deleted from all claims making the objection now moot.

**Claims 1-10 are rejected under 35USC112, first paragraph, because the specification does not reasonably provide enablement for an antibody, humanized antibody or antigen-binding fragment thereof that do not contain a full sent of 6 CDRs from the VH and the VL domains (3 from each) or comprise VH or VL regions consisting of amino acid sequences resulting from partial alterations of the sequences (e.g., SEQ ID NOS:1-8).** (Office Action p.4)

The language regarding partial alterations of the sequences has been deleted from all pending claims making this rejection now moot.

**Claim 1 is rejected under 35USC112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter with applicant regards as the invention**. (Office Action p.8)

Claim 1 has been canceled making this rejection now moot.

**Claims 1-6 are rejected under 35USC102(b) as being anticipated by Yanagisawa et al. (1997) FEBS Letters, 420: 43-46.** (Office Action p.8)

The limitation "the claimed antibody is a recombinant IgG, Fab, Fab', $F(ab')_2$, scFv, or dsFv" makes the amended claim 3 and the claims dependant thereon materially different from the antibody, which is denoted as 4396 antibody and is IgM class, disclosed by Yanagisawa et al. (1997) FEBS Letters, 420:43-46. In this respect, the antibody, as recited in amended claim 3, cannot legally be anticipated by Yanagisawa et al. (1997), which admittedly (Office Action p.10, text lines 20-21) does not disclose additional antibody binding forms, such as Fab, Fab', F(ab'), scFV or dsFv.

The invention as now claimed cannot possibly be anticipated by Yanagisawa et al. (1997). It is respectfully requested that the rejection be withdrawn.

**Claims 7-10 are rejected under 35USC103(a) as being unpatentable over Yanagisawa et al. (*FEBS Letters,* 1997; 420: 43-46), in view of US Patent No. 5,530,101 to Queen et al., 25 June 1996 and Webber et al. (*Mol Immunol,* 1995; 32(4): 249-258).** (Office Action p.10)

Claims 8-10 are canceled making this rejection moot with respect to these claims.

As explicitly explained in the specification of the present application at page 5, line 18 to page 6, line 10, the DNA sequence encoding the variable regions of the antibody 4396 were successfully determined by the inventors:

> Firstly, the **present inventors have identified the class of the antibody (antibody 4396) that recognizes GM1-bound Aβ. As a result, the class of the antibody was IgM and the L chain was a λ chain.** Then, the present inventors attempted to determine sequences of DNAs encoding variable regions of an H chain (heavy chain) and an L chain (light chain) and successfully determined the sequences thereof. Identification of DNA sequences of CDRs of the H chain and L chain was also

carried out. **Subsequently, a DNA encoding the H-chain variable region was synthesized and a DNA encoding a mouse IgG2a constant region were ligated and thereafter incorporated into an expression vector to form an H-chain expression vector.** Similarly, a vector into which a DNA encoding the L chain was incorporated (L-chain expression vector) was prepared. **These vectors were transfected into a CHO cell to form transformants.** Among the resultant transformants, a transformant with high capacity to produce antibodies was selected, and its culture supernatant was collected and purified. **Thus, an IgG antibody having a variable region of the antibody 4396 (hereinafter, also referred to as "antibody 4396C") was successfully obtained.** (emphasis added)

This achievement **allowed genetically manipulating the antibody resulting in obtaining a recombinant IgG class antibody**, i.e. antibody 4396C which falls into the scope of the amended claim 3. It is noteworthy that a recombinant antibody inhibited the formation of amyloid fibrils, in other words, suppression, of Aβ deposition (Examples 3 and 4 on p.43-46 of the specification). **In contrast, it was only binding affinity toward Aβ bound to lipid vesicles that had been revealed as to the 4396 antibody, which is IgM class. In this respect, a recombinant antibody as currently claimed could not have been anticipated, or even obvious to the art skilled person.** Further, Yanagisawa et al. (1997) does not disclose any information on the sequence of the antibody 4396 because the antibody 4396 had not been sequenced yet. The disclosure by Yanagisawa et al (1997) is, therefore, not sufficient at all for making a recombinant antibody as recited in the amended claim.

The combination of Yanagisawa, which admittedly does not teach humanized 4396 antibody or additional antibody binding forms, such as Fab, Fab', F(ab'), scFV or dsFv, in view of

Queen which teaches humanized antibodies and Webber, which teaches dsFv molecules, still **does not teach genetically manipulating the antibody resulting in obtaining a recombinant IgG class antibody.** Furthermore there is absolutely no teaching of a *humanized* antibody *being a recombinant IgG, Fab, Fab', F(ab')$_2$, scFv, or dsFv,* comprising: a heavy chain variable region; and a light chain variable region, wherein the heavy chain variable region comprises complementarity determining regions (CDRs) described in SEQ ID 1-3, and the light chain variable region comprises CDRs described in SEQ ID 4-6.

Advantageously, the claimed antibody of claim 7 shows a lower activity of non-specific absorption property and a far less tendency of aggregation because it is **an IgG class antibody or a fragment thereof, compared with the antibody 4396, which is IgM class.** This means that the claimed antibody is much more suitable for diagnostic and therapeutic use. Because there is no suggestion of this in the combination of references, the Examiner has not presented any motivation in the references for using an IgG class antibody.

In conclusion, it is logically impossible to derive the antibody of claim 7 from the combination of references because of the lack of motivation and teaching in the references. As a result, no *prima facie* teaching of obviousness can exist. It is respectfully requested that this rejection be reconsidered and withdrawn.

In view of the aforementioned amendments and accompanying remarks, claims 3-7, as amended, are in condition for allowance, which action, at an early date, is requested.

If, for any reason, it is felt that this application is not now in condition for allowance, the Examiner is requested to contact the applicants undersigned attorney at the telephone number indicated below to arrange for an interview to expedite the disposition of this case.

In the event that this paper is not timely filed, the applicants respectfully petition for an appropriate extension of time. Please charge any fees for such an extension of time and any other fees which may be due with respect to this paper, to Deposit Account No. 01-2340.

Respectfully submitted,

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